In claim 4, line 1, please replace "chlorotoxin-like compound" with --chlorotoxin ligand--.

REMARKS

The 35 USC §112 Rejection

Claims 1 and 4 stand rejected under 35 USC §112, second paragraph. This rejection is respectfully traversed.

The Examiner has argued that the definition of chlorotoxin-like protein "lacks metes and bounds." Accordingly, claims 1 and 4 have been amended as helpfully recommended by the Examiner. Therefore, the Applicants respectfully request that the 35 USC §112 rejection of Claims 1 and 4 be withdrawn.

The 35 USC §103(a) Rejections

Claims 1 and 4 stand rejected under 35 USC §103(a) as being unpatentable over **DeBin** et al. (Am. J. Physiol. 264/2, 33-2 (C361-C369), 1993) in view of **Weiss** et al. (U.S. Patent No: 5,750,376, May 12, 1998). This rejection is respectfully traversed.

DeBin et al. describes the purification and characterization of a chlorotoxin from the venom of the scorpion. **Weiss** teaches a method of producing genetically modified,

multipotent neural stem cells, in the course of which **Weiss** labels antibodies for Western blotting, radioimmune assays, an immunochemistry assay. The Examiner argues that it would be obvious for one of ordinary skill in the art to use the methods of **Weiss** to label the chlorotoxin taught by **DeBin** and use it for the detection of tumor cells. The Applicant respectfully disagrees.

Neither **DeBin** nor **Weiss** disclose that chlorotoxin binds to glial and meningioma derived tumor cells. **DeBin** only teaches that it binds to chloride channels present in epithelial cells, while **Weiss** makes no mention at all of chlorotoxin. No combination of the two references would lead one skilled in the art to conclude that chlorotoxin could be used as a diagnostic marker for tumor cells. With regard to claim 4, it is not the labeling of chlorotoxin that is the object of the claim but rather the use of the labeled chlorotoxin for the detection of glioma and meningioma tumor cells. While it might be obvious to label the chlorotoxin, it would not be obvious to use it for the diagnostic detection of these specific tumors. One skilled in the art would not know *a priori* that the chlorotoxin-sensitive chloride channels were specific to glioma and meningioma tumor cells rather than constitutively expressed in all glioma and meningioma tissues. Neither claim 1 nor 4 is rendered obvious by

the combination of **DeBin** and **Weiss**. Therefore, the applicants respectfully request that the 35 USC §103(a) rejection of claims 1 and 4 based on **DeBin** et al. in view of **Weiss** et al. be withdrawn.

The 35 USC §102 Rejections

Claim 1 has been rejected under 35 USC §102(a) as being anticipated by **Uchida** et al. (*J. Clin. Invest.*, 1, 104-13, Jan. 1995), or under 35 USC §102(b) as being anticipated by **DeBin** et al. (*Am. J. Physiol.* 264/2, 33-2 (C361-C369), 1993). These rejections are respectfully traversed.

Uchida et al. investigates the physiological role of a kidney-specific chloride channel, CIC-K1. To further these studies, antisera against CIC-K1 was developed which recognizes a 70 kD protein from the inner medulla of rat kidney. The Examiner argues that since the glioma chloride channel (GCC) is also 70 kD in size and was recognized by an antisera specific to CLC-5 from the kidney, then the CIC-K1 antisera will inherently recognize GCC. The Applicant respectfully disagrees.

Since both CIC-K1 and GCC are chloride channels and are about 70 kDa in size, the Examiner has presumed that they are the same protein. This is a highly speculative conclusion. First of all, 70

kDa is a fairly common size for proteins. In a large protein family such as that of chloride channels, it is likely that some members will be fairly similar in size. In addition, since CLC-5, CIC-K1, and GCC are all chloride channels, it is likely that they share some common features causing some degree of antisera cross reactivity even if the proteins are otherwise quite different. Furthermore, the Examiner is merely assuming that such cross reactivity exists. There is no actual evidence that the CIC-K1 antisera recognizes either CLC-5 or the GCC channel. While CIC-K1 and CLC-5 are both kidney chloride channels, they are different proteins and in fact, members of separate chloride channel families. Thus, even though CLC-5 antisera recognizes GCC, it does not follow that CIC-K1 antisera will as well. Finally, no mention was made in **Uchida** as to whether CIC-K1 is sensitive to chlorotoxin. Thus, the implication that CIC-K1 and GCC are the same protein is highly speculative and circumstantial.

DeBin et al. describes the purification and characterization of a chlorotoxin from the venom of the scorpion. To be an anticipatory reference under 35 USC §102a, the reference must be enabling to the same degree as the instant invention. **DeBin** fails to anticipate the instant invention in a number of ways. First, **DeBin** makes no suggestions of incorporating chlorotoxin in any kind of

pharmaceutical composition. While **DeBin** does describe chlorotoxin as blocking epithelial chloride channels, no reference is made to glial cells. **DeBin** does suggest that chlorotoxin may be useful for the purification and biophysical probing of chloride channels but does not make any proposals with regard to it having any possible therapeutic applications. Thus, neither Uchida nor DeBin anticipate the current invention. The Applicants respectfully request that the rejections of Claim 1 under 35 USC §102b as anticipated by **Uchida** et al. and under 35 USC §102b by **DeBin** et al. be withdrawn.

This is intended to be a complete response to the Office Action mailed December 10, 1999. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

Date: March 18, 1999

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